Resilience and Symmetry of the cerebral vasculature with regard to CAA

A graph theoretic model

Annual Multidisciplinary Meeting focused on Perivascular Drainage

Introduction

Alzheimer's disease (AD) is a debilitating medical condition that affects one in eight people over 65 years of age.

With ageing and certain genetic background soluble Aβ is not eliminated from the brain and it is deposited in the walls of blood vessels as cerebral amyloid angiopathy (CAA).

However, precise details of the mechanism of CAA are largely unknown.

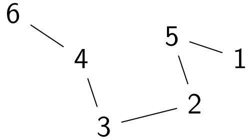
We build a graph theoretic model that demonstrates the importance of symmetry of the cerebral arterial tree to the proliferation of CAA.

Complex Networks

Q: What do social networks, the World Wide Web, the internet, *the cerebral vasculature* and epidemic models have in common?

A: They can all be thought of as networks/graphs with associated processes.

A graph, G, is a collection of 'points' called vertices, $V(G)$, and lines between these nodes called edges: $E(G)$.



Trees are an important type of graph. There is a unique shortest path between any pair of vertices.

Viewing the cerebral vasculature as a network

We can think of the cerebral arterial tree as an example.

The set of points where the arterial tree bifurcates correspond to vertices.

The blood vessels are the edges of this graph.

Similarly we can think of the basement membrane as a network.

The set of nodes of this network are the same as the nodes of the cerebral arterial tree.

However the edges of this graph correspond to the basement membrane surrounding cerebral arteries.

Resilience of Complex Networks

Given some complex network it is reasonable to ask if we remove vertices/edges either at random or specifically, what happens to this network.

Example

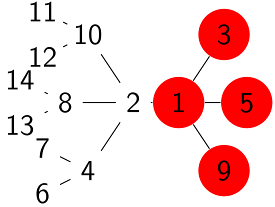
Albert *et al.* studied the effect of vertex deletion in a 326000-page subset of the World Wide Web.
They found the Web vulnerable to deliberate attack and resilient to random attack.

Albert *et al.* also found similar results for a subset of a representation of a subset of the internet, begging the question: is resilience related to the shape of the graph?

Symmetry of Complex Networks

- So how can we characterise the difference between G_1 and G_2?
- Given some tree T we can formally measure how *symmetric* that tree is by calculating the number of permutations of the vertices of that graph which preserves adjacent vertices.
- We call the set of all these permutations, $Aut(T)$, the *automorphism group* of T and the number of allowed permutations, $|Aut(T)|$ is the size of the automorphism group.

Consider the following increasing tree T_{14} with 14 vertices.



Figure

What we did

We used *matlab* to build a model which replicates CAA. The model is constituted of four processes:

(i) Generate a binary tree, T_n, on n nodes.

(ii) Calculate $|Aut(T_n)|$.

(iii) Dynamically remove edges of T_n according to a predetermined probability model.

(iv) Record the time, $\tau_{\frac{1}{2}}$, to remove half of the edges from T_n which we think of as the "half-life" of the process.

The Model of cerebral vasculature

We built a tree, T such that:

- T has 300 vertices and maximum degree 2.
- We associate each edge in T with an annular prism.
- We know the cross-sectional area of edges (corresponding to a capillaries) and every other edge's cross-sectional area can be derived from Murray's law adjusted for annular prisms.

$$r_p^3 = r_{d1}^3 + r_{d2}^3$$

So we know the volume, $Vol(e)$, of any edge $e \in E(T)$.

The Model of CAA

At time $t = 0$ we set $T(0)$ to be our randomly generated binary tree.

At time $t = 1, 2, \ldots$ for every edge we build $T(t)$ from $T(t-1)$ by defining a probability, P, that each edge is removed. Where P is defined in terms of concentration.

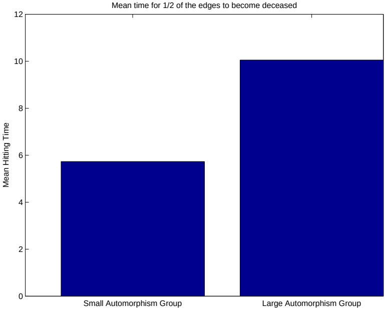
We assume that Aβ is produced at an approximately constant rate over our life time and that perivascular drainage is able to remove a constant quantity of $A\beta$ even in the face of adversity (the blockage of certain routes)

We define the concentration, $C(t)$, at time t to be $\frac{\text{initial volume}}{\text{current volume}}$.

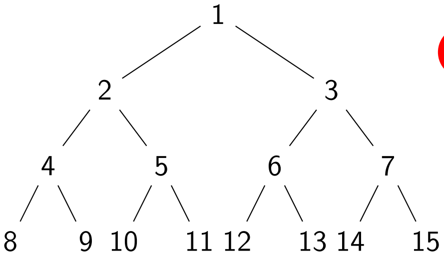
If edge $e = e_{uv}$ is removed then we also remove all branches further away from the root than e_{uv}.

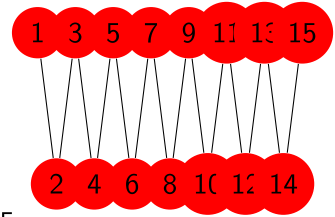
Results

The mean half-life of the generated trees.



An extreme example





$$\text{Expected time to remove edges from } G_1\text{: } 1\frac{8}{14} + 3\frac{4}{14} + 7\frac{2}{14} = \frac{12}{7} \tag{1}$$

$$\text{Expected time to remove edges from } G_2\text{: } \frac{1}{14}\sum_{k=1}^{14} k = \frac{15}{2} > \frac{12}{7} \tag{2}$$

Future Work

In order to improve the accuracy of our model we could make several modifications:

(i) Account for angiogenisis.

(ii) Fine tune the CAA deletion of node process.

(iii) Take into account the tortuous routes of perivascular drainage / the stiffening of arteries over time.

We also wish to verify the result by providing experimental evidence.

Comments and Questions